Clinical and Transvaginal Sonographic Evaluation of the Prostate in Transsexual Women

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OBJECTIVES To assess feasibility and diagnostic performance of prostate examination through transvaginal palpation and transvaginal ultrasound in transsexual women (TSW).

METHODS Fifty TSW who were at least 6 months' posttransition were recruited in a University Hospital. Speculum examination and digital vaginal examination were performed by a gynecologist. Transvaginal ultrasound of the prostate was performed by a radiologist. The information gathered included: ease of insertion of the speculum, vaginal length, palpability of the prostate, vaginal mobility and presence of scar tissue, ease of introduction of the ultrasound probe, ability to visualize prostate and seminal vesicles, echogenicity of the peripheral zone and the central gland, presence of calcifications and delineation of prostatic capsule, attitude toward gynecologic examinations, and anticipated and experienced painfulness of the different examinations.

RESULTS Speculum examination was possible in all but 1 patient and was easy in 78% of the patients. Median vaginal length was 7 cm. A regular digital vaginal examination was possible in 44% of the patients, the vagina was rather mobile and with limited scar tissue on average. In 48% of the patients, the prostate was palpable. In 94% of the patients, the prostate was visible on transvaginal ultrasound. Mean prostate volume was 14 mL, calcifications were present in 33%, and none had cysts. Capsule of the prostate was well delineated in 74% and seminal vesicles were visualized in 80%. All examinations were very well tolerated and nearly painless.

CONCLUSIONS Gynecologic examination and prostate assessment were acceptable to TSW. Transvaginal palpation of the prostate is of poor clinical value, yet transvaginal ultrasound allows for proper evaluation of the prostate status. UROLOGY 74: 191–196, 2009. © 2009 Elsevier Inc.

Transsexualism is the most extreme form of gender identity disorder[1] in which individuals need to adapt to their phenotype through hormonal treatment and sex reassignment surgery (SRS).[2] In male-to-female transsexual patients, denoted transsexual women (TSW), SRS typically involves removal of the external male reproductive organs and the construction of a neovagina and neoclitoris. Construction of the neovagina currently relies on inversion of the penile skin to line the newly created space between the pars fixa of the urethra and the rectum. The prostate and the seminal vesicles are left in place as to avoid the considerable short- and long-term morbidity associated with radical prostatectomy.

As SRS has become widely available and hence increasingly performed, follow-up of the prostate status may be warranted as part of the posttransition care for these patients. It may be acknowledged, however, that prostatic disease, including prostate carcinoma[3-7] and benign prostatic hyperplasia (BPH),[8-11] has been reported among TSW and that this new clinical entity will become more prevalent as more transsexual patients receive SRS.

Accordingly, in this study we assessed the feasibility and diagnostic performance of prostate examination through transvaginal palpation and ultrasound in a series of 50 transsexual patients.

MATERIALS AND METHODS

Patient Population

Dutch-speaking TSW who underwent genitoplasty at our center at least 6 months ago and who consulted 1 of the members of the gender team for treatment or follow-up during the past 12 months were invited to participate (n = 70). After 4 weeks, a participation rate of 50 of 70 (71%) participants was reached and no further efforts were made to increase the sample size. After written and oral informed consent, all participating

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women completed the study protocol between March and June 2007. The study complies with the recommendations of the Declaration of Helsinki and was approved by the local Ethical Committee (2006/375).

Study Procedures

Before the start of the examinations, the patients were interviewed by the study nurse about their attitude toward a "gynecologic check-up" and their expectations regarding painfulness of the examinations. Anticipated pain was scored on visual analogue scale (VAS) from 0-10. A fasting blood sample was taken for serum testosterone, estradiol, and prostate-specific antigen (PSA) measurements. PSA density of the prostate was calculated as the ratio of the PSA concentration (pg/mL) over the volume of the prostate (mL) as estimated on ultrasound.

Speculum and digital vaginal examinations were performed by a gynecologist who was previously not involved in the treatment or follow-up of TSW. Speculum examination was performed with a 10-cm long and 2.5-cm wide Collins speculum, or alternatively, a more slender (2.0 cm) Collins speculum, in case the insertion was judged too painful. The ease of insertion of the speculum was scored by the clinician from "easy" over "difficult" to "impossible."

A second speculum examination was performed with an extra long (12 cm) and slender (2.0 cm) fully lubricated speculum to assess the length of the vagina at full distension as allowed by the patient.

Similarly, a digital vaginal examination was performed with 1 or 2 fingers, depending on the perimeter of the vagina and the pain response of the patient. Accordingly, the mobility of the vaginal walls and the presence of scar tissue, rated on a scale from 0-3 (0 = immobile/no scar tissue, 1 = fairly rigid/minor scarring, 2 = mobile/moderate scarring, and 3 = very mobile/severe scarring) were assessed. In addition, the palpability and size of the prostate were recorded.

Transvaginal ultrasound was performed by an independent radiologist specialized in pelvic imaging. All examinations were performed with a 5-9 MHz endfire intracavitary probe on a high-end ultrasound machine (EUB-8500, Hitachi Medical Systems, Twinsburg, OH). Patients were imaged in the supine position, with hips in exorotation and knees gently bent. The parameters that were recorded included: ease of introduction of the ultrasound probe ("easy," "somewhat difficult," "difficult," or "impossible"), ability to visualize the prostate and seminal vesicles, echogenicity of the peripheral zone (PZ) and the central gland (CG) of prostatic tissue and the difference between both (CG/PZ differentiation), presence of calcifications, ability to sharply delineate the prostatic capsule and the prostatic volume as calculated using the ellipsoid formula (width $\times$ depth $\times$ height $\times$ 0.52).

The painfulness of the digital examination, the speculum examination and the transvaginal ultrasound examination were independently asked for by the clinician and by a study nurse and scored on a VAS scale.

During the conduct of the study, vaginal length proved on average significantly smaller compared with vaginal length assessed in the immediate posttransition phase, which probably relates to considerable differences in sexual behavior and dilatation habits. Accordingly, to assess vaginal length in a more standardized manner, patients were instructed to self-assess vaginal length after a standard protocol for dilatation of the neovagina (at least 5 minutes using sufficient lubricant and then to insert their prosthesis or a vibrator until they reached the top of the vagina). Patients were also asked for their dilatation habits through an additional questionnaire, which was handed to them at the end of the examinations.

Data Analysis

Distributions of continuous and discrete variables are summarized as means and standard deviations (SD) either as medians and interquartile range (IQ), depending on the consistency of the distributions with the normal distribution as explored through the 1-sample Kolmogorov-Smirnov test.

Similarly, bivariate correlations are represented by Pearson's R if the observed distribution approximated a normal distribution, either by Spearman's rank correlation coefficient rho under the nonparametric assumption.

Statistical significance was accepted at the conventional 2-tailed $\alpha = .05$ significance level. All analyses were performed with the statistical software package SPSS 15.0 (Chicago, IL).

RESULTS

Study Population Characteristics

Mean age of study participants was 43.1 years (SD = 10.4 years) and mean time elapsed since vaginoplasty was 6.3 years (SD = 6.4 years).

Nonparticipants (20) did not differ significantly for age distribution, surgical, or psychiatric morbidity compared with the 50 participants.

Blood Assays

The vast majority of participants were on estrogen replacement therapy. Three women were not taking any estrogens because they had an increased thromboembolic risk. Two women were combining estrogens with continuous antiandrogens (cyproterone acetate 10 mg daily).

Median serum levels for testosterone (ng/dL), estradiol (pg/dL), and PSA (ng/mL) were 29.57 (IQ range 21.45-38.24), 49.13 (IQ range 28.61-96.17), and 0.0300 (IQ range 0.0300-0.0815), respectively.

Patient Attitudes Toward the Examinations

Two patients previously experienced a speculum examination and 1 patient previously had a vaginal ultrasound examination, whereas none ever had a vaginal digital examination, albeit most women considered a regular vaginal examination (92%) and prostate examination (80%) desirable. Mean "anticipated pain" scores for speculum examination, digital vaginal examination, and vaginal ultrasound, on a 0-10 VAS was 4.09 (SD 2.80), 5.20 (SD 2.91), and 3.67 (SD 2.72), respectively.

Vaginal Digital and Speculum Examinations

A regular-sized speculum could be used in 37 women, whereas a small-sized speculum had to be used in the remainder; in 1 patient, insertion of a speculum was impossible because of the almost complete vaginal obliteration. Insertion was judged "easy" in 78%, and "difficult" among 20% of the study subjects. Mean vaginal length as measured by the clinician was 7.00 cm (SD 1.81).

Data on vaginal length as self-assessed after dilatation was obtained from 35 patients that resulted in a mean length of 9.80 cm (SD 2.77). All correlations are summarized in Table 1. A statistically significant positive correlation between the vaginal length as measured by the clinician and by the patient was observed, the latter value being consistently higher (mean difference = 3.00 cm, SD 2.19). Most patients (24/35) indicated that they dilate regularly or that they considered dilating obsolete because of regular intercourse. The remainder of patients indicated that they have refrained from dilatation because of pain.

A regular digital vaginal examination (with 2 fingers inserted in the vagina) was possible among 44% (22/50) of cases, whereas in the remainder, only 1 finger could readily be inserted (56%). The mean mobility of the vagina, as rated by the clinician on a scale from 0-3 was 1.70 (SD 0.71), that is, rather mobile on average. In particular, in 54% (27/50) of the women, the vagina was judged "mobile," in 32%, it was "fairly rigid," and in only 4%, the vagina was judged completely "immobile." Likewise, scar tissue was judged as being absent in 8% of the women, limited in 74%, whereas it was considered moderate to severe in 18%.

Significant negative correlations were observed between the presence of scar tissue and the size of the speculum that could be used, the physician-measured vaginal length and the mobility of the vagina. Conversely, the physician-measured vaginal length correlates positively with the mobility of the vagina.

In about half of the TSW (24/50), the prostate could be palpated transvaginally, though prostate size was consistently judged "small." There was no correlation between the palpability of the prostate and patient age. The palpability of the prostate, however, was significantly and positively correlated with the mobility and the physician-measured vaginal length.

After the gynecologic examination, the painfulness of the speculum and digital examinations was 2.48 (SD 2.21) and 1.80 (SD 1.99) when asked by the physician and 2.10 (SD 2.37) and 1.74 (SD 2.32) when asked by the study nurse, respectively.

Transvaginal Ultrasound of the Prostate

In all TSW, the prostate could be visualized using the endocavitary probe. Although in 3 patients, the vagina was too short to allow introduction of the tip of the probe, their prostate was sufficiently visualized transperineally. In 2 of these patients, visualization was insufficient to calculate the volume of the prostate reliably. Introduction of the probe was judged "easy" in 74% (37/50). The mean volume was 14.19 cm^3 (range 5-35, SD 5.95). There was a statistically significant positive correlation between the volume of the prostate on the one hand and serum value of PSA and the delineation of the prostate capsule on the other. The volume of the prostate, however, was not correlated with the duration of estrogen replacement therapy (available for 41 patients) nor with the interval since castration. Likewise, there was no correlation between the volume of the prostate and the age of the patient nor with the transvaginal palpation of the prostate.

The mean PSA-density (PSA/volume) was 0.00469 ($\pm$0.00590).

The CG/PZ differentiation was "good" in 70% (35/50) of the women; in 6%, it was "bad" or "not possible to define." The ultrasound pattern on CG was "normal" in 70%, "hypoechoic" in 6% and "hyperechoic" in 8%, whereas in 16%, it "could not be defined." On PZ, the pattern was "normal" in 82%, "hypoechoic" in 2%, and "hyperechoic" in 16%. Calcifications were present in 32% of the prostates and in none of the patients, were cysts present The capsule of the prostate was well delineated in 74% of the patients.The seminal vesicles were visualized in 80%. There was no correlation between the age of the patient and the presence of calcifications.

When asked for the painfulness of the vaginal ultrasound by the radiologist, the mean score on a VAS was 1.06 (SD 1.41); whereas it was 1.10 (SD 1.66) when asked for by the study nurse.

COMMENT

Vaginal palpation of the prostate was possible in merely half of the TSW. This was not explained by prostate size, which was consistently small (<35 mL), as previously documented in 2 historical case series of eunuchs[12] and by Van Kesteren et al.[13] Rather, palpability of the prostate was to a considerable extent explained by the length and the tissue rigidity of the neovagina.

In contrast, visualization of the prostate through transvaginal ultrasound proved feasible among 94% of patients, whereas proper imaging of seminal vesicles was obtained in 80% of the patients. Previous studies documented prostate assessment through transrectal,[14] abdominal, and perineal ultrasound[15] in rather small samples of TSW, whereas transvaginal ultrasound has only been reported anecdotically in a case of prostatitis[16] and in a series of 9 patients by Van Kesteren et al.,[13] although in the latter series, it is unclear to which extent findings relied on transvaginal or other modes of ultrasound.

Overall digital vaginal examination, speculum examination, and transvaginal ultrasound seemed to be well accepted by TSW, associated with low anticipated and experienced pain, and even considered desirable.

No gross anomalies of the prostate were observed in this case series. Calcifications of the prostate were apparent in 16 patients (32%), which concurs with age-stratified prevalences of 26.7% (4/15), 39.2% (11/32), and 33.3% (1/3) in TSW aged less than 40, 40-60, and older than 60 years respectively. In biologic men, calcifications in the prostate are considered as dystrophic and are therefore more frequently seen with increasing age (<25% before the age of 40 years, 40% between 40 and 60 years, and >75% in men older than 60 years).[17]

Table 1. Correlations

	Testosterone	E2	PSA	Prostate delineation capsula	Prostate calcifications	Prostate volume on US	Palpation of prostate possible	Mobility of vagina	Presence of scar tissue in vagina	Length of vagina by clinician	Size of speculum used	Duration estrogen therapy	Interval since castration	Age
Age														
Correlation Coefficient	−.188	−.064	−.050	.099	.213	.249	−.054	−.244	.177	−.281[a]	−.368[b]	.093	.322[a]	>.99
Significance[c]	.191	.657	.731	.494	.138	.088	.709	.087	.219	.048	.008	.561	.023	.
Interval since castration														
Correlation Coefficient	.170	−.251	−.029	.127	.198	−.070	.104	−.113	−.116	.047	−.251	.529[b]	>.99	
Significance	.238	.078	.842	.378	.169	.637	.472	.433	.423	.746	.078	.000	.	
Duration estrogen therapy														
Correlation Coefficient	.146	−.197	−.041	.201	.044	.126	.289	.114	−.072	.105	−.154	>.99		
Significance	.363	.216	.799	.207	.784	.437	.067	.478	.656	.512	.336	.		
Size of speculum used														
Correlation Coefficient	−.057	.204	−.094	−.327[a]	.012	−.323[a]	.204	.446[b]	−.536[b]	.583[b]	>.99			
Significance	.695	.156	.518	.020	.934	.025	.154	.001	.000	.000	.			
Length of vagina														
Correlation Coefficient	.268	−.007	−.034	−.072	033	−.228	.332[a]	.558[b]	−.568[b]	>.99				
Significance	.060	.962	.816	.617	.818	.119	.018	.000	.000	.				
Presence of scar tissue in vagina														
Correlation Coefficient	−.204	−.134	−.060	.353[a]	.043	.209	−.240	−.552[b]	>.99					
Significance	.156	.352	.677	.012	.766	.154	.094	.000	.					
Mobility of vagina														
Correlation Coefficient	.187	.036	.002	−.178	−.044	−.093	.396[b]	>.99						
Significance	.192	.804	.987	.217	.764	.530	.004	.						
Palpation of prostate possible														
Correlation Coefficient	.405[b]	−.080	.347[a]	−.042	.351[a]	.164	>.99							
Significance	.004	.579	.013	.774	.012	.264	.							
Prostate volume measured on US														
Correlation Coefficient	−.087	.192	.362[a]	.526[b]	−.124	>.99								
Significance	.557	.191	.012	.000	.403	.								
Prostate calcifications														
Correlation Coefficient	−.004	−.209	−.070	−.095	>.99									
Significance	.978	.146	.627	.511	.									
Prostate delination capsula														
Correlation Coefficient	−.049	−.048	−.015	>.99										
Significance	.738	.740	.919	.										

Table 1. continued.

	Testosterone	E2	PSA	Prostate delineation capsula	Prostate calcifications	Prostate volume on US	Palpation of prostate possible	Mobility of vagina	Presence of scar tissue in vagina	Length of vagina by clinician	Size of speculum used	Duration estrogen therapy	Interval since castration	Age
PSA														
Correlation Coefficient	.316[a]	.139	>.99											
Significance	.025	.337	.											
E2														
Correlation Coefficient	.023	>.99												
Significance	.876													
Testosterone														
Correlation Coefficient	>.99													
Significance	.													

E2 = estradiol; PSA = prostate-specific antigen; US = ultrasound.
[a] Correlation is significant at the .05 level.
[b] Correlation is significant at the .01 level.
[c] 2-tailed.

Prostatic cysts, being a common finding among biologic men, were not observed among TSW. This finding probably results from the limited sample size.

Clearly, prostate volume and PSA levels are considerably lower than in biologic men of corresponding age and, hence, also well below the diagnostic cutoff values for prostatic disease. This finding was not quite unexpected, as all patients have been castrated and present with low testosterone levels, whereas, in addition, most of these patients are on estrogen replacement therapy. This finding is in accordance with the small case series by Van Kesteren et al.,[13] who reported prostatic volumes of <20 mL and PSA levels mostly below 0.1 ng/mL among 9 castrated TSW.

In BPH, prostate size is known to decrease about 30% with castration or with the use of androgen-blocking agents.[18] Moreover, castration before the age of 40 years has shown to prevent the development of BPH and prostatic cancer because androgens regulate prostate cancer cell growth.[19,20]

On the other hand, it may be acknowledged that although estrogens have gonadotropin-suppressive effects causing androgen withdrawal, female hormones have actually been implicated in the development of BPH and prostate cancer. Estrogen receptors are present in the prostate and with increasing age, the estrogen/testosterone ratio equally increases.[21] New evidence has become available that estrogens, alone or in synergism with androgens, can induce aberrant growth and neoplastic transformation in the prostate. The mechanisms of estrogen carcinogenicity are not completely clear yet, but are probably mediated via induction of unscheduled cell proliferation or through metabolic activation of estrogens to genotoxic metabolites.[22]

Jin et al.[14] showed that in 14 TSW, all taking estrogens, but 10 of which had not been castrated, the mean prostatic volume, as measured transrectally, was significantly lower than among age-matched controls (19.3 mL vs 28.2 mL, $P < .001$), thereby documenting the net effect of estrogen substitution on prostate volume. We observed, however, no significant influence of the duration of estrogen intake or the interval since the castration on the volume of the prostate. Nor was there a relation between the volume of the prostate and the serum levels of estrogen or total testosterone—as observed by Jin et al.—or with the estrogen/testosterone ratio.

Prostate volume, as expected, significantly correlated with circulating PSA levels, but not with age, contrary to this well-known association among biologic men.[23,24]

From the previous discussion, it may be concluded that castration, but even more so, estrogen replacement therapy suppresses prostatic growth also with increasing age. As a straightforward corollary, TSW could be assumed to have a considerably lower risk of BPH and prostatic cancer developing than their male counterparts.

Nevertheless, prostatic disease has been reported in TSW and therefore regular screening from the age of 50

years on could be considered, assuming that such screening would be found cost-effective. It may be acknowledged indeed that screening for prostate cancer is under much debate even for biologic men,[25] and therefore some restraint in applying screening examinations is appropriate in TSW.

In conclusion, we found that gynecologic examination and prostate assessment was largely acceptable to TSW. We further showed that transvaginal palpation of the prostate is of poor clinical value, whereas conversely transvaginal ultrasound is feasible and allows for proper evaluation of the prostate status. If prostatic enlargement is suspected transvaginal ultrasound is probably the first designated imaging examination.

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